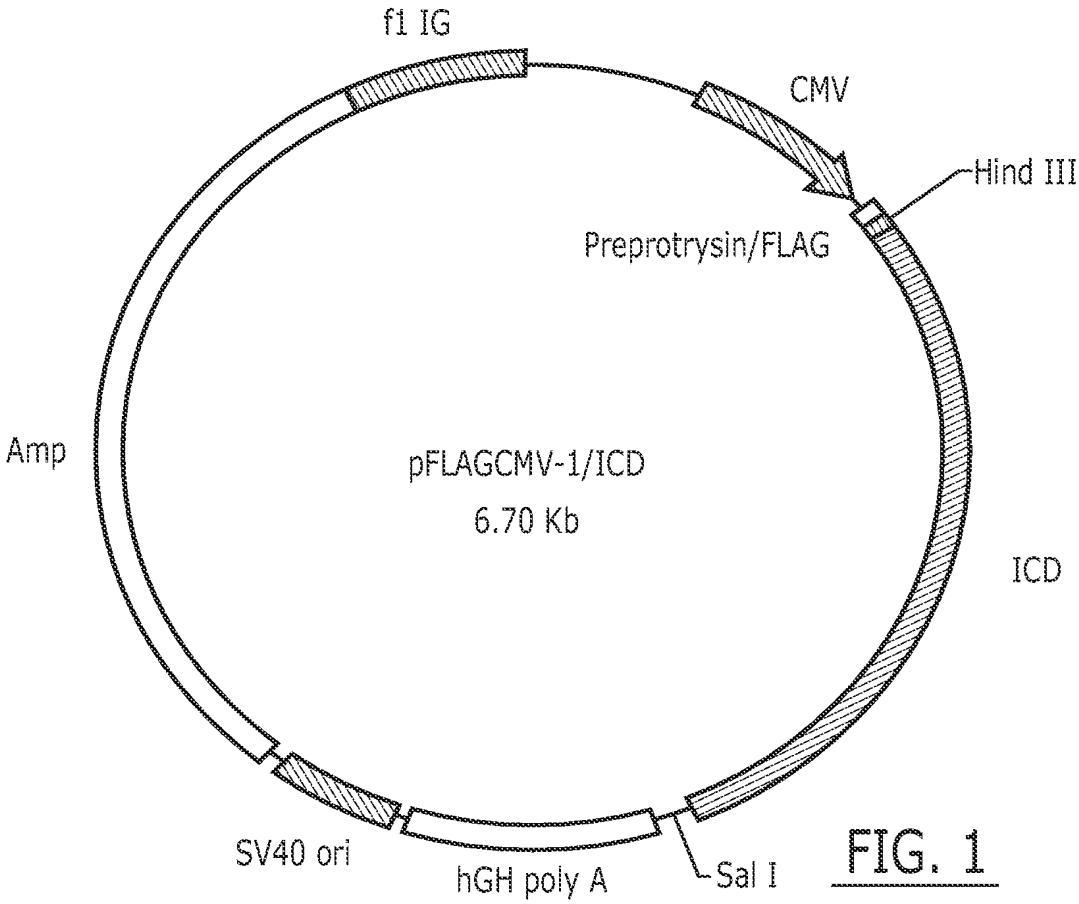
f1 IG
CMV
Hind III
Preprotrysin/FLAG
Amp
pFLAGCMV-1/ICD
6.70 Kb
ICD
SV40 ori
hGH poly A
Sal I

FIG. 1

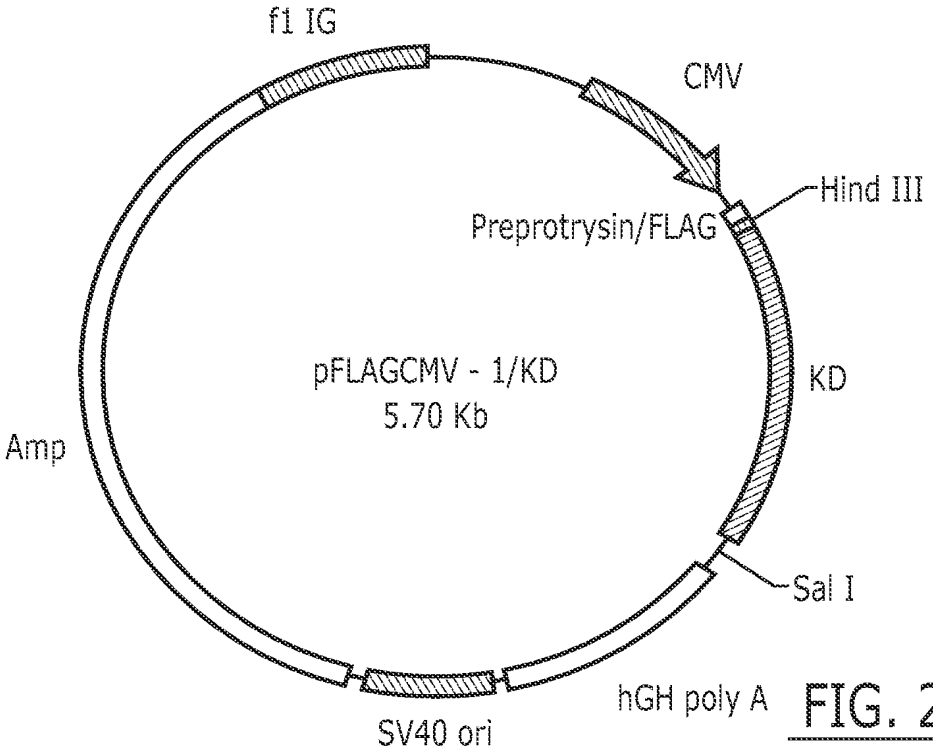
f1 IG
CMV
Hind III
Preprotrysin/FLAG
pFLAGCMV - 1/KD
5.70 Kb
KD
Amp
Sal I
hGH poly A
SV40 ori

FIG. 2

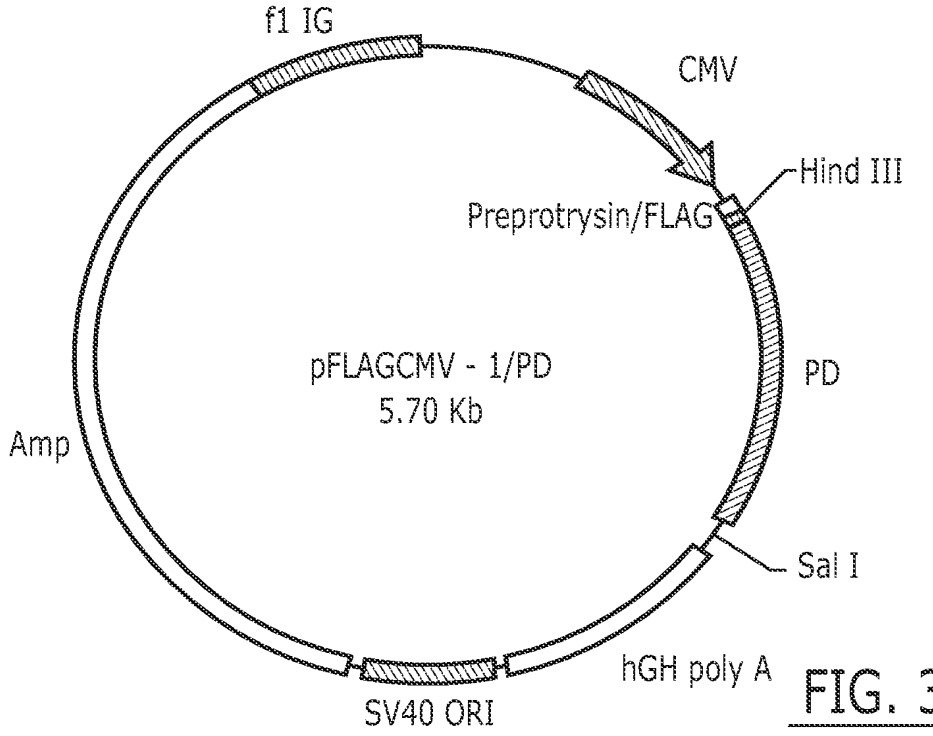
f1 IG
CMV
Hind III
Preprotrysin/FLAG
pFLAGCMV - 1/PD
5.70 Kb
PD
Amp
Sal I
hGH poly A
SV40 ORI

FIG. 3

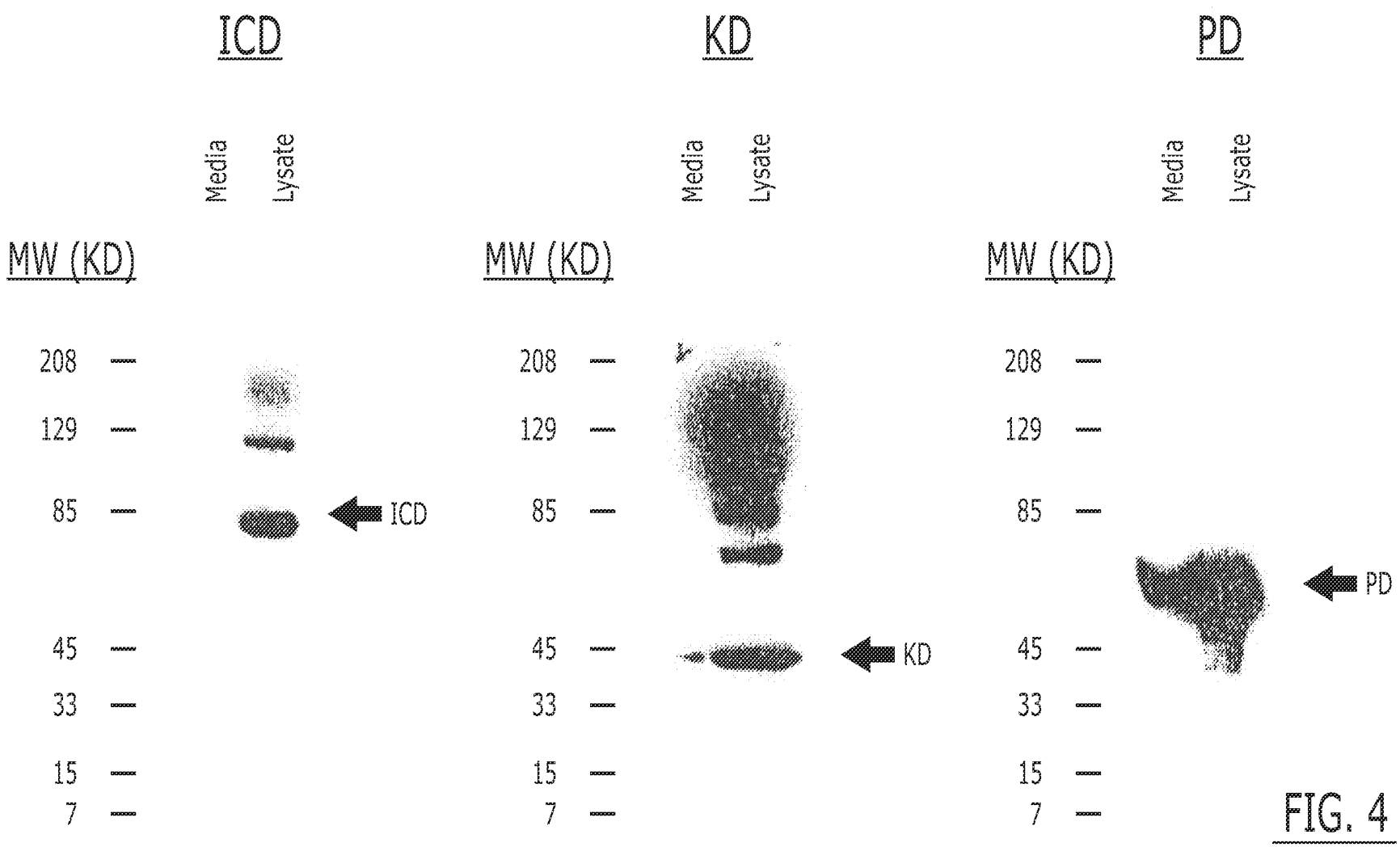
ICD
Media
Lysate
MW (KD)
208
129
85
45
33
15
7
ICD
KD
Media
Lysate
MW (KD)
208
129
85
45
33
15
7
KD
PD
Media
Lysate
MW (KD)
208
129
85
45
33
15
7
PD

FIG. 4

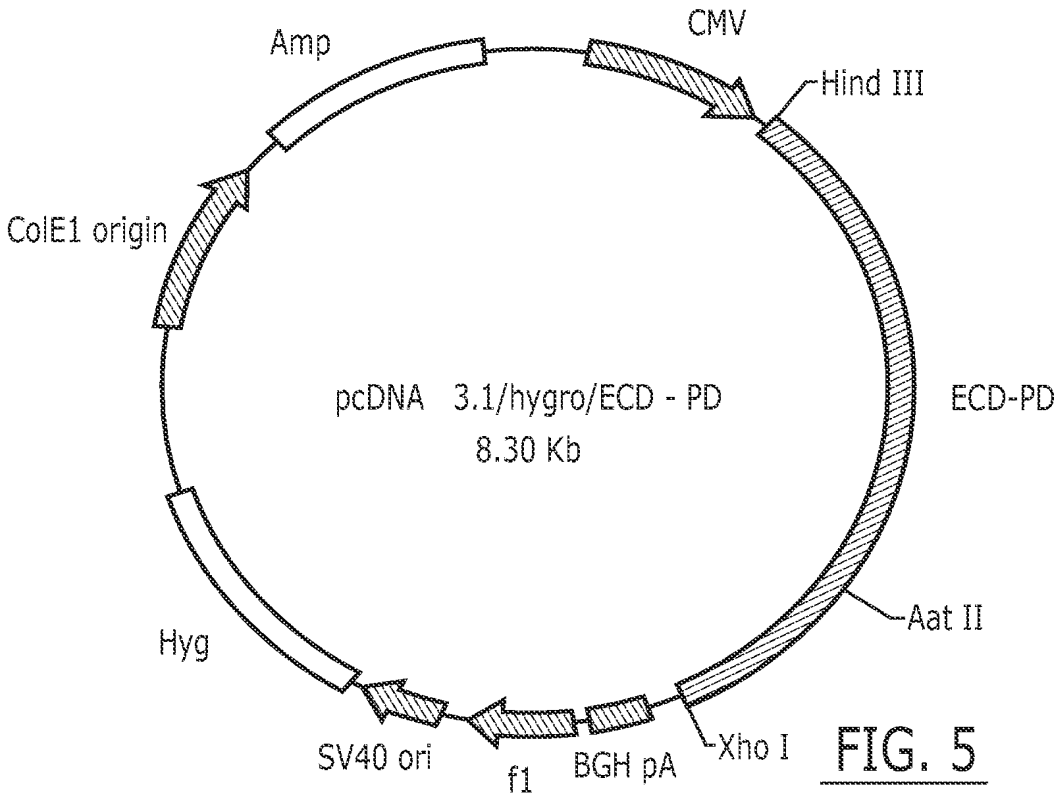
Amp
CMV
Hind III
ColE1 origin
pcDNA 3.1/hygro/ECD - PD
8.30 Kb
ECD-PD
Aat II
Hyg
SV40 ori
f1
BGH pA
Xho I

FIG. 5

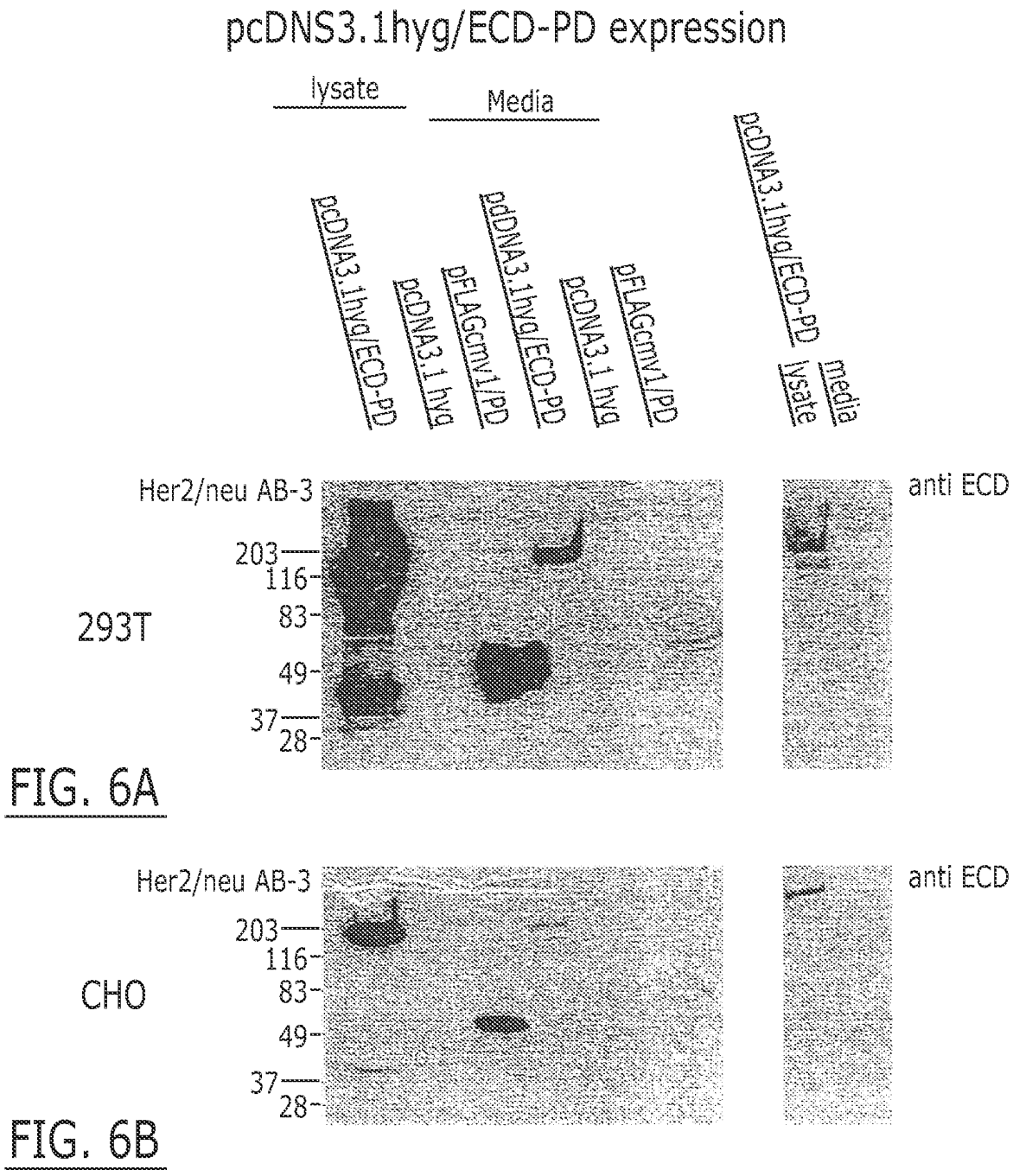
pcDNS3.1hyg/ECD-PD expression
lysate
Media
pcDNA3.1hyg/ECD-PD
pcDNA3.1 hyg
pFLAGcmv1/PD
pdDNA3.1hyg/ECD-PD
pcDNA3.1 hyg
pFLAGcmv1/PD
pcDNA3.1hyg/ECD-PD
lysate
media
Her2/neu AB-3
anti ECD
293T
203
116
83
49
37
28
Her2/neu AB-3
anti ECD
CHO
203
116
83
49
37
28

FIG. 6A

FIG. 6B

Fig. 7a (SEQ ID NO:1)

```
Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu Pro Pro Gly Ala  20
Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys Leu Arg Leu Pro Ala Ser Pro Glu  40
Thr His Leu Asp Met Leu Arg His Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu  60
Glu Leu Thr Tyr Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val  80
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu Gln Arg Leu Arg  100

Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr Ala Leu Ala Val Leu Asp Asn Gly  120
Asp Pro Leu Asn Asn Thr Thr Pro Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu  140
Gln Leu Arg Ser Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln  160
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn Asn Gln Leu Ala  180
Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys His Pro Cys Ser Pro Met Cys Lys  200

Gly Ser Arg Cys Trp Gly Glu Ser Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys  220
Ala Gly Gly Cys Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys  240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu His Phe Asn His  260
Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val Thr Tyr Asn Thr Asp Thr Phe Glu  280
Ser Met Pro Asn Pro Glu Gly Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro  300

Tyr Asn Tyr Leu Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln  320
Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys Pro Cys Ala Arg  340
Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu Val Arg Ala Val Thr Ser Ala Asn  360
Ile Gln Glu Phe Ala Gly Cys Lys Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser  380
Phe Asp Gly Asp Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe  400

Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Pro  420
Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg Gly Arg Ile Leu His Asn Gly Ala  440
Tyr Ser Leu Thr Leu Gln Gly Leu Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu  460
Leu Gly Ser Gly Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val  480
Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr Ala Asn Arg Pro  500

Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His Gln Leu Cys Ala Arg Gly His Cys  520
Trp Gly Pro Gly Pro Thr Gln Cys Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys  540
Val Glu Glu Cys Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys  560
Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys Phe Gly Pro Glu  580
Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp Pro Pro Phe Cys Val Ala Arg Cys  600

Pro Ser Gly Val Lys Pro Asp Leu Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu 620
Gly Ala Cys Gln Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys 640
Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Ile Ile Ser Ala Val Val Gly 660
Ile Leu Leu Val Val Val Leu Gly Val Val Phe Gly Ile Leu Ile Lys Arg Arg Gln Gln 680
Lys Ile Arg Lys Tyr Thr Met Arg Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu 700

Thr Pro Ser Gly Ala Met Pro Asn Gln Ala Gln Met Arg Ile Leu Lys Glu Thr Glu Leu 720
Arg Lys Val Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr Lys Gly Ile Trp Ile 740
Pro Asp Gly Glu Asn Val Lys Ile Pro Val Ala Ile Lys Val Leu Arg Glu Asn Thr Ser 760
Pro Lys Ala Asn Lys Glu Ile Leu Asp Glu Ala Tyr Val Met Ala Gly Val Gly Ser Pro 780
Tyr Val Ser Arg Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Val Thr Gln Leu 800
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Fig. 7b (SEQ ID NO:1)

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Met Pro Tyr Gly Cys Leu Leu Asp His Val Arg Glu Asn Arg Gly Arg Leu Gly Ser Gln 820
Asp Leu Leu Asn Trp Cys Met Gln Ile Ala Lys Gly Met Ser Tyr Leu Glu Asp Val Arg 840

Leu Val His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys 860
Ile Thr Asp Phe Gly Leu Ala Arg Leu Leu Asp Ile Asp Glu Thr Glu Tyr His Ala Asp 880
Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu Arg Arg Arg Phe Thr 900

His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Val Trp Glu Leu Met Thr Phe Gly Ala 920
Lys Pro Tyr Asp Gly Ile Pro Ala Arg Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg 940
Leu Pro Gln Pro Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp Met 960
Ile Asp Ser Glu Cys Arg Pro Arg Phe Arg Glu Leu Val Ser Glu Phe Ser Arg Met Ala 980
Arg Asp Pro Gln Arg Phe Val Val Ile Gln Asn Glu Asp Leu Gly Pro Ala Ser Pro Leu 1000


Asp Ser Thr Phe Tyr Arg Ser Leu Leu Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala 1020
Glu Glu Tyr Leu Val Pro Gln Gln Gly Phe Phe Cys Pro Asp Pro Ala Pro Gly Ala Gly 1040
Gly Met Val His His Arg His Arg Ser Ser Ser Thr Arg Ser Gly Gly Gly Asp Leu Thr 1060
Leu Gly Leu Glu Pro Ser Glu Glu Glu Ala Pro Arg Ser Pro Leu Ala Pro Ser Glu Gly 1080
Ala Gly Ser Asp Val Phe Asp Gly Asp Leu Gly Met Gly Ala Ala Lys Gly Leu Gln Ser 1100


Leu Pro Thr His Asp Pro Ser Pro Leu Gln Arg Tyr Ser Glu Asp Pro Thr Val Pro Leu 1120
Pro Ser Glu Thr Asp Gly Tyr Val Ala Pro Leu Thr Cys Ser Pro Gln Pro Glu Tyr Val 1140
Asn Gln Pro Asp Val Arg Pro Gln Pro Pro Ser Pro Arg Glu Gly Pro Leu Pro Ala Ala 1160
Arg Pro Ala Gly Ala Thr Leu Glu Arg Pro Lys Thr Leu Ser Pro Gly Lys Asn Gly Val 1180
Val Lys Asp Val Phe Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr Leu Thr Pro Gln 1200

Gly Gly Ala Ala Pro Gln Pro His Pro Pro Pro Ala Phe Ser Pro Ala Phe Asp Asn Leu 1220
Tyr Tyr Trp Asp Gln Asp Pro Pro Glu Arg Gly Ala Pro Pro Ser Thr Phe Lys Gly Thr 1240
Pro Thr Ala Glu Asn Pro Glu Tyr Leu Gly Leu Asp Val Pro Val  .   .      1257
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REPLACEMENT SHEET
Title: HER-2/NEU Fusion Proteins
Inventor: Cheever et al.
Attorney Docket No. CRX113US

Figure 8a (SEQ ID NO: 2)

Met Glu Leu Ala Ala Trp Cys Arg Trp Gly Phe Leu Leu Ala Leu Leu Pro Pro Gly Ile	20
Ala Gly Thr Gln Val Cys Thr Gly Thr Asp Met Lys Leu Arg Leu Pro Ala Ser Pro Glu	40
Thr His Leu Asp Met Leu Arg His Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu	60
Glu Leu Thr Tyr Val Pro Ala Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val	80
Gln Gly Tyr Met Leu Ile Ala His Asn Gln Val Lys Arg Val Pro Leu Gln Arg Leu Arg	100
Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Lys Tyr Ala Leu Ala Val Leu Asp Asn Arg	120
Asp Pro Gln Asp Asn Val Ala Ala Ser Thr Pro Gly Arg Thr Pro Glu Gly Leu Arg Glu	140
Leu Gln Leu Arg Ser Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Arg Gly Asn Pro	160
Gln Leu Cys Tyr Gln Asp Met Val Leu Trp Lys Asp Val Phe Arg Lys Asn Asn Gln Leu	180
Ala Pro Val Asp Ile Asp Thr Asn Arg Ser Arg Ala Cys Pro Pro Cys Ala Pro Ala Cys	200
Lys Asp Asn His Cys Trp Gly Glu Ser Pro Glu Asp Cys Gln Ile Leu Thr Gly Thr Ile	220
Cys Thr Ser Gly Cys Ala Arg Cys Lys Gly Arg Leu Pro Thr Asp Cys Cys His Glu Gln	240
Cys Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu His Phe Asn	260
His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val Thr Tyr Asn Thr Asp Thr Phe	280
Glu Ser Met His Asn Pro Glu Gly Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Thr Cys	300
Pro Tyr Asn Tyr Leu Ser Thr Glu Val Gly Ser Cys Thr Leu Val Cys Pro Pro Asn Asn	320
Gln Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys Pro Cys Ala	340
Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Gly Ala Arg Ala Ile Thr Ser Asp	360
Asn Val Gln Glu Phe Asp Gly Cys Lys Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu	380
Ser Phe Asp Gly Asp Pro Ser Ser Gly Ile Ala Pro Leu Arg Pro Glu Gln Leu Gln Val	400
Phe Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu	420
Arg Asp Leu Ser Val Phe Gln Asn Leu Arg Ile Ile Arg Gly Arg Ile Leu His Asp Gly	440
Ala Tyr Ser Leu Thr Leu Gln Gly Leu Gly Ile His Ser Leu Gly Leu Arg Ser Leu Arg	460
Glu Leu Gly Ser Gly Leu Ala Leu Ile His Arg Asn Ala His Leu Cys Phe Val His Thr	480
Val Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Ser Gly Asn Arg	500
Pro Glu Glu Asp Cys Gly Leu Glu Gly Leu Val Cys Asn Ser Leu Cys Ala His Gly His	520
Cys Trp Gly Pro Gly Pro Thr Gln Cys Val Asn Cys Ser His Phe Leu Arg Gly Gln Glu	540
Cys Val Glu Glu Cys Arg Val Trp Lys Gly Leu Pro Arg Glu Tyr Val Ser Asp Lys Arg	560
Cys Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Ser Ser Glu Thr Cys Phe Gly Ser	580
Glu Ala Asp Gln Cys Ala Ala Cys Ala His Tyr Lys Asp Ser Ser Ser Cys Val Ala Arg	600
Cys Pro Ser Gly Val Lys Pro Asp Leu Ser Tyr Met Pro Ile Trp Lys Tyr Pro Asp Glu	620
Glu Gly Ile Cys Gln Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Glu	640
Arg Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Val Thr Phe Ile Ile Ala Thr Val Val	660
Gly Val Leu Leu Phe Leu Ile Leu Val Val Val Val Gly Ile Leu Ile Lys Arg Arg Arg	680
Gln Lys Ile Arg Lys Tyr Thr Met Arg Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro	700
Leu Thr Pro Ser Gly Ala Met Pro Asn Gln Ala Gln Met Arg Ile Leu Lys Glu Thr Glu	720
Leu Arg Lys Val Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr Lys Gly Ile Trp	740
Ile Pro Asp Gly Glu Asn Val Lys Ile Pro Val Ala Ile Lys Val Leu Arg Glu Asn Thr	760
Ser Pro Lys Ala Asn Lys Glu Ile Leu Asp Glu Ala Tyr Val Met Ala Gly Val Gly Ser	780
Pro Tyr Val Ser Arg Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Val Thr Gln	800

Figure 8b SEQ ID NO :2	
Leu Met Pro Tyr Gly Cys Leu Leu Asp His Val Arg Glu His Arg Gly Arg Leu Gly Ser	820
Gln Asp Leu Leu Asn Trp Cys Val Gln Ile Ala Lys Gly Met Ser Tyr Leu Glu Asp Val	840
Arg Leu Val His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Lys Ser Pro Asn His Val	860
Lys Ile Thr Asp Phe Gly Leu Ala Arg Leu Leu Asp Ile Asp Glu Thr Glu Tyr His Ala	880
Asp Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu Arg Arg Arg Phe	900
Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Val Trp Glu Leu Met Thr Phe Gly	920
Ala Lys Pro Tyr Asp Gly Ile Pro Ala Arg Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu	940
Arg Leu Pro Gln Pro Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp	960
Met Ile Asp Ser Glu Cys Arg Pro Arg Phe Arg Glu Leu Val Ser Glu Phe Ser Arg Met	980
Ala Arg Asp Pro Gln Arg Phe Val Val Ile Gln Asn Glu Asp Leu Gly Pro Ser Ser Pro	1000
Met Asp Ser Thr Phe Tyr Arg Ser Leu Leu Glu Asp Asp Asp Met Gly Asp Leu Val Asp	1020
Ala Glu Glu Tyr Leu Val Pro Gln Gln Gly Phe Phe Ser Pro Asp Pro Thr Pro Gly Thr	1040
Gly Ser Thr Ala His Arg Arg His Arg Ser Ser Ser Thr Arg Ser Gly Gly Gly Glu Leu	1060
Thr Leu Gly Leu Glu Pro Ser Glu Glu Gly Pro Pro Arg Ser Pro Leu Ala Pro Ser Glu	1080
Gly Ala Gly Ser Asp Val Phe Asp Gly Asp Leu Ala Met Gly Val Thr Lys Gly Leu Gln	1100
Ser Leu Ser Pro His Asp Leu Ser Pro Leu Gln Arg Tyr Ser Glu Asp Pro Thr Leu Pro	1120
Leu Pro Pro Glu Thr Asp Gly Tyr Val Ala Pro Leu Ala Cys Ser Pro Gln Pro Glu Tyr	1140
Val Asn Gln Ser Glu Val Gln Pro Gln Pro Pro Leu Thr Pro Glu Gly Pro Leu Pro Pro	1160
Val Arg Pro Ala Gly Ala Thr Leu Glu Arg Pro Lys Thr Leu Ser Pro Gly Lys Asn Gly	1180
Val Val Lys Asp Val Phe Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr Leu Val Pro	1200
Arg Glu Gly Thr Ala Ser Pro Pro His Pro Ser Pro Ala Phe Ser Pro Ala Phe Asp Asn	1220
Leu Tyr Tyr Trp Asp Gln Asn Ser Ser Glu Gln Gly Pro Pro Pro Ser Asn Phe Glu Gly	1240
Thr Pro Thr Ala Glu Asn Pro Glu Tyr Leu Gly Leu Asp Val Pro Val . . 1258	

REPLACEMENT SHEET
Title: HER-2/NEU Fusion Proteins
Inventor: Cheever et al.
Attorney Docket No. CRX113US

Figure 9 (SEQ ID NO: 3)

Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu Pro Pro Gly Ala	20
Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys Leu Arg Leu Pro Ala Ser Pro Glu	40
Thr His Leu Asp Met Leu Arg His Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu	60
Glu Leu Thr Tyr Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val	80
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu Gln Arg Leu Arg	100
Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr Ala Leu Ala Val Leu Asp Asn Gly	120
Asp Pro Leu Asn Asn Thr Thr Pro Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu	140
Gln Leu Arg Ser Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln	160
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn Asn Gln Leu Ala	180
Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys His Pro Cys Ser Pro Met Cys Lys	200
Gly Ser Arg Cys Trp Gly Glu Ser Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys	220
Ala Gly Gly Cys Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys	240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu His Phe Asn His	260
Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val Thr Tyr Asn Thr Asp Thr Phe Glu	280
Ser Met Pro Asn Pro Glu Gly Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro	300
Tyr Asn Tyr Leu Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln	320
Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys Pro Cys Ala Arg	340
Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu Val Arg Ala Val Thr Ser Ala Asn	360
Ile Gln Glu Phe Ala Gly Cys Lys Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser	380
Phe Asp Gly Asp Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe	400
Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Pro	420
Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg Gly Arg Ile Leu His Asn Gly Ala	440
Tyr Ser Leu Thr Leu Gln Gly Leu Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu	460
Leu Gly Ser Gly Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val	480
Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr Ala Asn Arg Pro	500
Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His Gln Leu Cys Ala Arg Gly His Cys	520
Trp Gly Pro Gly Pro Thr Gln Cys Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys	540
Val Glu Glu Cys Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys	560
Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys Phe Gly Pro Glu	580
Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp Pro Pro Phe Cys Val Ala Arg Cys	600
Pro Ser Gly Val Lys Pro Asp Leu Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu	620
Gly Ala Cys Gln Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys	640
Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser 653	

Figure 10 (SEQ ID NO: 4)

Gln Asn Glu Asp Leu Gly Pro Ala Ser Pro Leu Asp Ser Thr Phe Tyr Arg Ser Leu Leu	20
Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala Glu Glu Tyr Leu Val Pro Gln Gln Gly	40
Phe Phe Cys Pro Asp Pro Ala Pro Gly Ala Gly Gly Met Val His His Arg His Arg Ser	60
Ser Ser Thr Arg Ser Gly Gly Gly Asp Leu Thr Leu Gly Leu Glu Pro Ser Glu Glu Glu	80
Ala Pro Arg Ser Pro Leu Ala Pro Ser Glu Gly Ala Gly Ser Asp Val Phe Asp Gly Asp	100
Leu Gly Met Gly Ala Ala Lys Gly Leu Gln Ser Leu Pro Thr His Asp Pro Ser Pro Leu	120
Gln Arg Tyr Ser Glu Asp Pro Thr Val Pro Leu Pro Ser Glu Thr Asp Gly Tyr Val Ala	140
Pro Leu Thr Cys Ser Pro Gln Pro Glu Tyr Val Asn Gln Pro Asp Val Arg Pro Gln Pro	160
Pro Ser Pro Arg Glu Gly Pro Leu Pro Ala Ala Arg Pro Ala Gly Ala Thr Leu Glu Arg	180
Pro Lys Thr Leu Ser Pro Gly Lys Asn Gly Val Val Lys Asp Val Phe Ala Phe Gly Gly	200
Ala Val Glu Asn Pro Glu Tyr Leu Thr Pro Gln Gly Gly Ala Ala Pro Gln Pro His Pro	220
Pro Pro Ala Phe Ser Pro Ala Phe Asp Asn Leu Tyr Tyr Trp Asp Gln Asp Pro Pro Glu	240
Arg Gly Ala Pro Pro Ser Thr Phe Lys Gly Thr Pro Thr Ala Glu Asn Pro Glu Tyr Leu	260
Gly Leu Asp Val Pro Val . 267	

Figure 11 (SEQ ID NO: 5)

Gln Asn Glu Asp Leu Gly Pro Ala Ser Pro Leu Asp Ser Thr Phe Tyr Arg Ser Leu Leu	20
Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala Glu Glu Tyr Leu Val Pro Gln Gln Gly	40
Phe Phe Cys Pro Asp Pro Ala Pro Gly Ala Gly Gly Met Val His His Arg His Arg .	60

Figure 12 (SEQ ID NO: 6)

Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu Pro Pro Gly Ala	20
Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys Leu Arg Leu Pro Ala Ser Pro Glu	40
Thr His Leu Asp Met Leu Arg His Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu	60
Glu Leu Thr Tyr Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val	80
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu Gln Arg Leu Arg	100
Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr Ala Leu Ala Val Leu Asp Asn Gly	120
Asp Pro Leu Asn Asn Thr Thr Pro Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu	140
Gln Leu Arg Ser Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln	160
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn Asn Gln Leu Ala	180
Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys His Pro Cys Ser Pro Met Cys Lys	200
Gly Ser Arg Cys Trp Gly Glu Ser Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys	220
Ala Gly Gly Cys Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys	240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu His Phe Asn His	260
Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val Thr Tyr Asn Thr Asp Thr Phe Glu	280
Ser Met Pro Asn Pro Glu Gly Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro	300
Tyr Asn Tyr Leu Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln	320
Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys Pro Cys Ala Arg	340
Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu Val Arg Ala Val Thr Ser Ala Asn	360
Ile Gln Glu Phe Ala Gly Cys Lys Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser	380
Phe Asp Gly Asp Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe	400
Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Pro	420
Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg Gly Arg Ile Leu His Asn Gly Ala	440
Tyr Ser Leu Thr Leu Gln Gly Leu Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu	460
Leu Gly Ser Gly Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val	480
Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr Ala Asn Arg Pro	500
Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His Gln Leu Cys Ala Arg Gly His Cys	520
Trp Gly Pro Gly Pro Thr Gln Cys Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys	540
Val Glu Glu Cys Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys	560
Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys Phe Gly Pro Glu	580
Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp Pro Pro Phe Cys Val Ala Arg Cys	600
Pro Ser Gly Val Lys Pro Asp Leu Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu	620
Gly Ala Cys Gln Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys	640
Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Gln Asn Glu Asp Leu Gly Pro	660
Ala Ser Pro Leu Asp Ser Thr Phe Tyr Arg Ser Leu Leu Glu Asp Asp Asp Met Gly Asp	680
Leu Val Asp Ala Glu Glu Tyr Leu Val Pro Gln Gln Gly Phe Phe Cys Pro Asp Pro Ala	700
Pro Gly Ala Gly Gly Met Val His His Arg His Arg Ser Ser Ser Thr Arg Ser Gly Gly	720
Gly Asp Leu Thr Leu Gly Leu Glu Pro Ser Glu Glu Glu Ala Pro Arg Ser Pro Leu Ala	740
Pro Ser Glu Gly Ala Gly Ser Asp Val Phe Asp Gly Asp Leu Gly Met Gly Ala Ala Lys	760
Gly Leu Gln Ser Leu Pro Thr His Asp Pro Ser Pro Leu Gln Arg Tyr Ser Glu Asp Pro	780
Thr Val Pro Leu Pro Ser Glu Thr Asp Gly Tyr Val Ala Pro Leu Thr Cys Ser Pro Gln	800
Pro Glu Tyr Val Asn Gln Pro Asp Val Arg Pro Gln Pro Pro Ser Pro Arg Glu Gly Pro	820
Leu Pro Ala Ala Arg Pro Ala Gly Ala Thr Leu Glu Arg Pro Lys Thr Leu Ser Pro Gly	840
Lys Asn Gly Val Val Lys Asp Val Phe Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr	860
Leu Thr Pro Gln Gly Gly Ala Ala Pro Gln Pro His Pro Pro Pro Ala Phe Ser Pro Ala	880
Phe Asp Asn Leu Tyr Tyr Trp Asp Gln Asp Pro Pro Glu Arg Gly Ala Pro Pro Ser Thr	900
Phe Lys Gly Thr Pro Thr Ala Glu Asn Pro Glu Tyr Leu Gly Leu Asp Val Pro Val .	920

REPLACEMENT SHEET
Title: HER-2/NEU Fusion Proteins
Inventor: Cheever et al.
Attorney Docket No. CRX113US

Figure 13 (SEQ ID NO: 7)

Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu Pro Pro Gly Ala	20
Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys Leu Arg Leu Pro Ala Ser Pro Glu	40
Thr His Leu Asp Met Leu Arg His Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu	60
Glu Leu Thr Tyr Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val	80
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu Gln Arg Leu Arg	100
Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr Ala Leu Ala Val Leu Asp Asn Gly	120
Asp Pro Leu Asn Asn Thr Thr Pro Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu	140
Gln Leu Arg Ser Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln	160
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn Asn Gln Leu Ala	180
Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys His Pro Cys Ser Pro Met Cys Lys	200
Gly Ser Arg Cys Trp Gly Glu Ser Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys	220
Ala Gly Gly Cys Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys	240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu His Phe Asn His	260
Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val Thr Tyr Asn Thr Asp Thr Phe Glu	280
Ser Met Pro Asn Pro Glu Gly Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro	300
Tyr Asn Tyr Leu Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln	320
Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys Pro Cys Ala Arg	340
Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu Val Arg Ala Val Thr Ser Ala Asn	360
Ile Gln Glu Phe Ala Gly Cys Lys Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser	380
Phe Asp Gly Asp Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe	400
Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Pro	420
Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg Gly Arg Ile Leu His Asn Gly Ala	440
Tyr Ser Leu Thr Leu Gln Gly Leu Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu	460
Leu Gly Ser Gly Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val	480
Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr Ala Asn Arg Pro	500
Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His Gln Leu Cys Ala Arg Gly His Cys	520
Trp Gly Pro Gly Pro Thr Gln Cys Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys	540
Val Glu Glu Cys Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys	560
Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys Phe Gly Pro Glu	580
Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp Pro Pro Phe Cys Val Ala Arg Cys	600
Pro Ser Gly Val Lys Pro Asp Leu Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu	620
Gly Ala Cys Gln Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys	640
Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Gln Asn Glu Asp Leu Gly Pro	660
Ala Ser Pro Leu Asp Ser Thr Phe Tyr Arg Ser Leu Leu Glu Asp Asp Asp Met Gly Asp	680
Leu Val Asp Ala Glu Glu Tyr Leu Val Pro Gln Gln Gly Phe Phe Cys Pro Asp Pro Ala	700
Pro Gly Ala Gly Gly Met Val His His Arg His Arg . . 714	

REPLACEMENT SHEET
Title: HER-2/NEU Fusion Proteins
Inventor: Cheever et al.
Attorney Docket No. CRX113US

Figure 14 (SEQ ID NO: 8)

Met Glu Leu Ala Ala Trp Cys Arg Trp Gly Phe Leu Leu Ala Leu Leu Pro Pro Gly Ile	20
Ala Gly Thr Gln Val Cys Thr Gly Thr Asp Met Lys Leu Arg Leu Pro Ala Ser Pro Glu	40
Thr His Leu Asp Met Leu Arg His Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu	60
Glu Leu Thr Tyr Val Pro Ala Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val	80
Gln Gly Tyr Met Leu Ile Ala His Asn Gln Val Lys Arg Val Pro Leu Gln Arg Leu Arg	100
Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Lys Tyr Ala Leu Ala Val Leu Asp Asn Arg	120
Asp Pro Gln Asp Asn Val Ala Ala Ser Thr Pro Gly Arg Thr Pro Glu Gly Leu Arg Glu	140
Leu Gln Leu Arg Ser Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Arg Gly Asn Pro	160
Gln Leu Cys Tyr Gln Asp Met Val Leu Trp Lys Asp Val Phe Arg Lys Asn Asn Gln Leu	180
Ala Pro Val Asp Ile Asp Thr Asn Arg Ser Arg Ala Cys Pro Pro Cys Ala Pro Ala Cys	200
Lys Asp Asn His Cys Trp Gly Glu Ser Pro Glu Asp Cys Gln Ile Leu Thr Gly Thr Ile	220
Cys Thr Ser Gly Cys Ala Arg Cys Lys Gly Arg Leu Pro Thr Asp Cys Cys His Glu Gln	240
Cys Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu His Phe Asn	260
His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val Thr Tyr Asn Thr Asp Thr Phe	280
Glu Ser Met His Asn Pro Glu Gly Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Thr Cys	300
Pro Tyr Asn Tyr Leu Ser Thr Glu Val Gly Ser Cys Thr Leu Val Cys Pro Pro Asn Asn	320
Gln Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys Pro Cys Ala	340
Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Gly Ala Arg Ala Ile Thr Ser Asp	360
Asn Val Gln Glu Phe Asp Gly Cys Lys Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu	380
Ser Phe Asp Gly Asp Pro Ser Ser Gly Ile Ala Pro Leu Arg Pro Glu Gln Leu Gln Val	400
Phe Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu	420
Arg Asp Leu Ser Val Phe Gln Asn Leu Arg Ile Ile Arg Gly Arg Ile Leu His Asp Gly	440
Ala Tyr Ser Leu Thr Leu Gln Gly Leu Gly Ile His Ser Leu Gly Leu Arg Ser Leu Arg	460
Glu Leu Gly Ser Gly Leu Ala Leu Ile His Arg Asn Ala His Leu Cys Phe Val His Thr	480
Val Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Ser Gly Asn Arg	500
Pro Glu Glu Asp Cys Gly Leu Glu Gly Leu Val Cys Asn Ser Leu Cys Ala His Gly His	520
Cys Trp Gly Pro Gly Pro Thr Gln Cys Val Asn Cys Ser His Phe Leu Arg Gly Gln Glu	540
Cys Val Glu Glu Cys Arg Val Trp Lys Gly Leu Pro Arg Glu Tyr Val Ser Asp Lys Arg	560
Cys Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Ser Ser Glu Thr Cys Phe Gly Ser	580
Glu Ala Asp Gln Cys Ala Ala Cys Ala His Tyr Lys Asp Ser Ser Ser Cys Val Ala Arg	600
Cys Pro Ser Gly Val Lys Pro Asp Leu Ser Tyr Met Pro Ile Trp Lys Tyr Pro Asp Glu	620
Glu Gly Ile Cys Gln Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Glu	640
Arg Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Val Thr Phe 654	

FIGURE 15a (SEQ ID NO:9)

```
atg gag ctg gcg gcc ttg tgc cgc tgg ggg ctc ctc ctc gcc ctc ttg       48
Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
1               5                  10                  15

ccc ccc gga gcc gcg agc acc caa gtg tgc acc ggc aca gac atg aag       96
Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
            20                  25                  30

ctg cgg ctc cct gcc agt ccc gag acc cac ctg gac atg ctc cgc cac      144
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
        35                  40                  45

ctc tac cag ggc tgc cag gtg gtg cag gga aac ctg gaa ctc acc tac      192
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
    50                  55                  60

ctg ccc acc aat gcc agc ctg tcc ttc ctg cag gat atc cag gag gtg      240
Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65                  70                  75                  80

cag ggc tac gtg ctc atc gct cac aac caa gtg agg cag gtc cca ctg      288
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
                85                  90                  95

cag agg ctg cgg att gtg cga ggc acc cag ctc ttt gag gac aac tat      336
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
            100                 105                 110

gcc ctg gcc gtg cta gac aat gga gac ccg ctg aac aat acc acc cct      384
Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
        115                 120                 125

gtc aca ggg gcc tcc cca gga ggc ctg cgg gag ctg cag ctt cga agc      432
Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
    130                 135                 140

ctc aca gag atc ttg aaa gga ggg gtc ttg atc cag cgg aac ccc cag      480
Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145                 150                 155                 160

ctc tgc tac cag gac acg att ttg tgg aag gac atc ttc cac aag aac      528
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
                165                 170                 175

aac cag ctg gct ctc aca ctg ata gac acc aac cgc tct cgg gcc tgc      576
Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
            180                 185                 190

cac ccc tgt tct ccg atg tgt aag ggc tcc cgc tgc tgg gga gag agt      624
His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
        195                 200                 205
```

Figure 15b (SEQ ID NO: 9)

```
tct gag gat tgt cag agc ctg acg cgc act gtc tgt gcc ggt ggc tgt      672
Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
    210                 215                 220

gcc cgc tgc aag ggg cca ctg ccc act gac tgc tgc cat gag cag tgt      720
Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225                 230                 235                 240

gct gcc ggc tgc acg ggc ccc aag cac tct gac tgc ctg gcc tgc ctc      768
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
                245                 250                 255

cac ttc aac cac agt ggc atc tgt gag ctg cac tgc cca gcc ctg gtc      816
His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
            260                 265                 270

acc tac aac aca gac acg ttt gag tcc atg ccc aat ccc gag ggc cgg      864
Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
        275                 280                 285

tat aca ttc ggc gcc agc tgt gtg act gcc tgt ccc tac aac tac ctt      912
Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
    290                 295                 300

tct acg gac gtg gga tcc tgc acc ctc gtc tgc ccc ctg cac aac caa      960
Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305                 310                 315                 320

gag gtg aca gca gag gat gga aca cag cgg tgt gag aag tgc agc aag     1008
Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
                325                 330                 335

ccc tgt gcc cga gtg tgc tat ggt ctg ggc atg gag cac ttg cga gag     1056
Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu
            340                 345                 350

gtg agg gca gtt acc agt gcc aat atc cag gag ttt gct ggc tgc aag     1104
Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys
        355                 360                 365

aag atc ttt ggg agc ctg gca ttt ctg ccg gag agc ttt gat ggg gac     1152
Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp
    370                 375                 380

cca gcc tcc aac act gcc ccg ctc cag cca gag cag ctc caa gtg ttt     1200
Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe
385                 390                 395                 400

gag act ctg gaa gag atc aca ggt tac cta tac atc tca gca tgg ccg     1248
Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro
                405                 410                 415
```

Figure 15c (SEQ ID NO: 9)

```
gac agc ctg cct gac ctc agc gtc ttc cag aac ctg caa gta atc cgg     1296
Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg
            420                 425                 430

gga cga att ctg cac aat ggc gcc tac tcg ctg acc ctg caa ggg ctg     1344
Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu
        435                 440                 445

ggc atc agc tgg ctg ggg ctg cgc tca ctg agg gaa ctg ggc agt gga     1392
Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly
    450                 455                 460

ctg gcc ctc atc cac cat aac acc cac ctc tgc ttc gtg cac acg gtg     1440
Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val
465                 470                 475                 480

ccc tgg gac cag ctc ttt cgg aac ccg cac caa gct ctg ctc cac act     1488
Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr
                485                 490                 495

gcc aac cgg cca gag gac gag tgt gtg ggc gag ggc ctg gcc tgc cac     1536
Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His
            500                 505                 510

cag ctg tgc gcc cga ggg cac tgc tgg ggt cca ggg ccc acc cag tgt     1584
Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys
        515                 520                 525

gtc aac tgc agc cag ttc ctt cgg ggc cag gag tgc gtg gag gaa tgc     1632
Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys
    530                 535                 540

cga gta ctg cag ggg ctc ccc agg gag tat gtg aat gcc agg cac tgt     1680
Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys
545                 550                 555                 560

ttg ccg tgc cac cct gag tgt cag ccc cag aat ggc tca gtg acc tgt     1728
Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys
                565                 570                 575

ttt gga ccg gag gct gac cag tgt gtg gcc tgt gcc cac tat aag gac     1776
Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp
            580                 585                 590

cct ccc ttc tgc gtg gcc cgc tgc ccc agc ggt gtg aaa cct gac ctc     1824
Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu
        595                 600                 605

tcc tac atg ccc atc tgg aag ttt cca gat gag gag ggc gca tgc cag     1872
Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln
    610                 615                 620
```

Figure 15d (SEQ ID NO: 9)

```
cct tgc ccc atc aac tgc acc cac tcc tgt gtg gac ctg gat gac aag     1920
Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys
625                 630                 635                 640

ggc tgc ccc gcc gag cag aga gcc agc cct ctg acg tcc atc atc tct     1968
Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Ile Ile Ser
                645                 650                 655

gcg gtg gtt ggc att ctg ctg gtc gtg gtc ttg ggg gtg gtc ttt ggg     2016
Ala Val Val Gly Ile Leu Leu Val Val Val Leu Gly Val Val Phe Gly
            660                 665                 670

atc ctc atc aag cga cgg cag cag aag atc cgg aag tac acg atg cgg     2064
Ile Leu Ile Lys Arg Arg Gln Gln Lys Ile Arg Lys Tyr Thr Met Arg
        675                 680                 685

aga ctg ctg cag gaa acg gag ctg gtg gag ccg ctg aca cct agc gga     2112
Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser Gly
    690                 695                 700

gcg atg ccc aac cag gcg cag atg cgg atc ctg aaa gag acg gag ctg     2160
Ala Met Pro Asn Gln Ala Gln Met Arg Ile Leu Lys Glu Thr Glu Leu
705                 710                 715                 720

agg aag gtg aag gtg ctt gga tct ggc gct ttt ggc aca gtc tac aag     2208
Arg Lys Val Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr Lys
                725                 730                 735

ggc atc tgg atc cct gat ggg gag aat gtg aaa att cca gtg gcc atc     2256
Gly Ile Trp Ile Pro Asp Gly Glu Asn Val Lys Ile Pro Val Ala Ile
            740                 745                 750

aaa gtg ttg agg gaa aac aca tcc ccc aaa gcc aac aaa gaa atc tta     2304
Lys Val Leu Arg Glu Asn Thr Ser Pro Lys Ala Asn Lys Glu Ile Leu
        755                 760                 765

gac gaa gca tac gtg atg gct ggt gtg ggc tcc cca tat gtc tcc cgc     2352
Asp Glu Ala Tyr Val Met Ala Gly Val Gly Ser Pro Tyr Val Ser Arg
    770                 775                 780

ctt ctg ggc atc tgc ctg aca tcc acg gtg cag ctg gtg aca cag ctt     2400
Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Val Thr Gln Leu
785                 790                 795                 800

atg ccc tat ggc tgc ctc tta gac cat gtc cgg gaa aac cgc gga cgc     2448
Met Pro Tyr Gly Cys Leu Leu Asp His Val Arg Glu Asn Arg Gly Arg
                805                 810                 815

ctg ggc tcc cag gac ctg ctg aac tgg tgt atg cag att gcc aag ggg     2496
Leu Gly Ser Gln Asp Leu Leu Asn Trp Cys Met Gln Ile Ala Lys Gly
            820                 825                 830
```

Figure 15e (SEQ ID NO: 9)

```
atg agc tac ctg gag gat gtg cgg ctc gta cac agg gac ttg gcc gct     2544
Met Ser Tyr Leu Glu Asp Val Arg Leu Val His Arg Asp Leu Ala Ala
        835                 840                 845

cgg aac gtg ctg gtc aag agt ccc aac cat gtc aaa att aca gac ttc     2592
Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys Ile Thr Asp Phe
    850                 855                 860

ggg ctg gct cgg ctg ctg gac att gac gag aca gag tac cat gca gat     2640
Gly Leu Ala Arg Leu Leu Asp Ile Asp Glu Thr Glu Tyr His Ala Asp
865                 870                 875                 880

ggg ggc aag gtg ccc atc aag tgg atg gcg ctg gag tcc att ctc cgc     2688
Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu Arg
                885                 890                 895

cgg cgg ttc acc cac cag agt gat gtg tgg agt tat ggt gtg act gtg     2736
Arg Arg Phe Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Val
            900                 905                 910

tgg gag ctg atg act ttt ggg gcc aaa cct tac gat ggg atc cca gcc     2784
Trp Glu Leu Met Thr Phe Gly Ala Lys Pro Tyr Asp Gly Ile Pro Ala
        915                 920                 925

cgg gag atc cct gac ctg ctg gaa aag ggg gag cgg ctg ccc cag ccc     2832
Arg Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln Pro
    930                 935                 940

ccc atc tgc acc att gat gtc tac atg atc atg gtc aaa tgt tgg atg     2880
Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp Met
945                 950                 955                 960

att gac tct gaa tgt cgg cca aga ttc cgg gag ttg gtg tct gaa ttc     2928
Ile Asp Ser Glu Cys Arg Pro Arg Phe Arg Glu Leu Val Ser Glu Phe
                965                 970                 975

tcc cgc atg gcc agg gac ccc cag cgc ttt gtg gtc atc cag aat gag     2976
Ser Arg Met Ala Arg Asp Pro Gln Arg Phe Val Val Ile Gln Asn Glu
            980                 985                 990

gac ttg ggc cca gcc agt ccc ttg  gac agc acc ttc tac  cgc tca ctg   3024
Asp Leu Gly Pro Ala Ser Pro Leu  Asp Ser Thr Phe Tyr  Arg Ser Leu
        995                 1000                1005

ctg gag  gac gat gac atg ggg  gac ctg gtg gat gct  gag gag tat      3069
Leu Glu  Asp Asp Asp Met Gly  Asp Leu Val Asp Ala  Glu Glu Tyr
    1010                1015                1020

ctg gta  ccc cag cag ggc ttc  ttc tgt cca gac cct  gcc ccg ggc      3114
Leu Val  Pro Gln Gln Gly Phe  Phe Cys Pro Asp Pro  Ala Pro Gly
    1025                1030                1035
```

Figure 15f (SEQ ID NO: 9)

```
gct ggg  ggc atg gtc cac cac  agg cac cgc agc tca  tct acc agg      3159
Ala Gly  Gly Met Val His His  Arg His Arg Ser Ser  Ser Thr Arg
    1040                 1045                 1050

agt ggc  ggt ggg gac ctg aca  cta ggg ctg gag ccc  tct gaa gag      3204
Ser Gly  Gly Gly Asp Leu Thr  Leu Gly Leu Glu Pro  Ser Glu Glu
    1055                 1060                 1065

gag gcc  ccc agg tct cca ctg  gca ccc tcc gaa ggg  gct ggc tcc      3249
Glu Ala  Pro Arg Ser Pro Leu  Ala Pro Ser Glu Gly  Ala Gly Ser
    1070                 1075                 1080

gat gta  ttt gat ggt gac ctg  gga atg ggg gca gcc  aag ggg ctg      3294
Asp Val  Phe Asp Gly Asp Leu  Gly Met Gly Ala Ala  Lys Gly Leu
    1085                 1090                 1095

caa agc  ctc ccc aca cat gac  ccc agc cct cta cag  cgg tac agt      3339
Gln Ser  Leu Pro Thr His Asp  Pro Ser Pro Leu Gln  Arg Tyr Ser
    1100                 1105                 1110

gag gac  ccc aca gta ccc ctg  ccc tct gag act gat  ggc tac gtt      3384
Glu Asp  Pro Thr Val Pro Leu  Pro Ser Glu Thr Asp  Gly Tyr Val
    1115                 1120                 1125

gcc ccc  ctg acc tgc agc ccc  cag cct gaa tat gtg  aac cag cca      3429
Ala Pro  Leu Thr Cys Ser Pro  Gln Pro Glu Tyr Val  Asn Gln Pro
    1130                 1135                 1140

gat gtt  cgg ccc cag ccc cct  tcg ccc cga gag ggc  cct ctg cct      3474
Asp Val  Arg Pro Gln Pro Pro  Ser Pro Arg Glu Gly  Pro Leu Pro
    1145                 1150                 1155

gct gcc  cga cct gct ggt gcc  act ctg gaa agg ccc  aag act ctc      3519
Ala Ala  Arg Pro Ala Gly Ala  Thr Leu Glu Arg Pro  Lys Thr Leu
    1160                 1165                 1170

tcc cca  ggg aag aat ggg gtc  gtc aaa gac gtt ttt  gcc ttt ggg      3564
Ser Pro  Gly Lys Asn Gly Val  Val Lys Asp Val Phe  Ala Phe Gly
    1175                 1180                 1185

ggt gcc  gtg gag aac ccc gag  tac ttg aca ccc cag  gga gga gct      3609
Gly Ala  Val Glu Asn Pro Glu  Tyr Leu Thr Pro Gln  Gly Gly Ala
    1190                 1195                 1200

gcc cct  cag ccc cac cct cct  cct gcc ttc agc cca  gcc ttc gac      3654
Ala Pro  Gln Pro His Pro Pro  Pro Ala Phe Ser Pro  Ala Phe Asp
    1205                 1210                 1215

aac ctc  tat tac tgg gac cag  gac cca cca gag cgg  ggg gct cca      3699
Asn Leu  Tyr Tyr Trp Asp Gln  Asp Pro Pro Glu Arg  Gly Ala Pro
    1220                 1225                 1230
```

Figure 15g (SEQ ID NO: 9)

```
ccc agc  acc ttc aaa ggg aca  cct acg gca gag aac  cca gag tac      3744
Pro Ser  Thr Phe Lys Gly Thr  Pro Thr Ala Glu Asn  Pro Glu Tyr
    1235                 1240                 1245

ctg ggt  ctg gac gtg cca gtg  tga                                  3768
Leu Gly  Leu Asp Val Pro Val
    1250                 1255
```

FIGURE 16a (SEQ ID NO: 10)

```
   1 ccgggccgga gccgcaatga tcatcatgga gctggcggcc tggtgccgct gggggttcct
  61 cctcgccctc ctgccccccg gaatcgcggg cacccaagtg tgtaccggca cagacatgaa
 121 gttgcggctc cctgccagtc ctgagaccca cctggacatg ctccgccacc tgtaccaggg
 181 ctgtcaggta gtgcagggca acttggagct tacctacgtg cctgccaatg ccagcctctc
 241 attcctgcag gacatccagg aagttcaggg ttacatgctc atcgctcaca accaggtgaa
 301 gcgcgtccca ctgcaaaggc tgcgcatcgt gagagggacc cagctctttg aggacaagta
 361 tgccctggct gtgctagaca accgagatcc tcaggacaat gtcgccgcct ccaccccagg
 421 cagaacccca gaggggctgc gggagctgca gcttcgaagt ctcacagaga tcctgaaggg
 481 aggagttttg atccgtggga accctcagct ctgctaccag gacatggttt tgtggaagga
 541 cgtcttccgc aagaataacc aactggctcc tgtcgatata gacaccaatc gttcccgggc
 601 ctgtccacct tgtgcccccg cctgcaaaga caatcactgt tggggtgaga gtccggaaga
 661 ctgtcagatc ttgactggca ccatctgtac cagtggttgt gcccggtgca agggccggct
 721 gcccactgac tgctgccatg agcagtgtgc cgcaggctgc acgggcccca agcattctga
 781 ctgcctggcc tgcctccact tcaatcatag tggtatctgt gagctgcact gcccagccct
 841 cgtcacctac aacacagaca cctttgagtc catgcacaac cctgagggtc gctacacctt
 901 tggtgccagc tgcgtgacca cctgccccta caactacctg tctacggaag tgggatcctg
 961 cactctggtg tgtcccccga ataaccaaga ggtcacagct gaggacggaa cacagcgttg
1021 tgagaaatgc agcaagccct gtgctcgagt gtgctatggt ctgggcatgg agcaccttcg
1081 aggggcgagg gccatcacca gtgacaatgt ccaggagttt gatggctgca agaagatctt
1141 tgggagcctg gcatttttgc cggagagctt tgatggggac ccctcctccg gcattgctcc
1201 gctgaggcct gagcagctcc aagtgttcga aaccctggag gagatcacag gttacctgta
1261 catctcagca tggccagaca gtctccgtga cctcagtgtc ttccagaacc ttcgaatcat
1321 tcggggacgg attctccacg atggcgcgta ctcattgaca ctgcaaggcc tggggatcca
1381 ctcgctgggg ctgcgctcac tgcgggagct gggcagtgga ttggctctga ttcaccgcaa
1441 cgcccatctc tgctttgtac acactgtacc ttgggaccag ctcttccgga acccacatca
1501 ggccctgctc cacagtggga accggccgga agaggacttg tgcgtctcga gcggcttggt
1561 ctgtaactca ctgtgtgccc acgggcactg ctgggggcca gggcccaccc agtgtgtcaa
1621 ctgcagtcat ttccttcggg gccaggagtg tgtggaggag tgccgagtat ggaaggggct
1681 cccccgggag tatgtgagtg acaagcgctg tctgccgtgt caccccgagt gtcagcctca
1741 aaacagctca gagacctgct ttggatcgga ggctgatcag tgtgcagcct gcgcccacta
1801 caaggactcg tcctcctgtg tggctcgctg ccccagtggt gtgaaaccgg acctctccta
1861 catgcccatc tggaagtacc cggatgagga gggcatatgc cagccgtgcc ccatcaactg
1921 cacccactcc tgtgtggatc tggatgaacg aggctgccca gcagagcaga gagccagccc
1981 ggtgacattc atcattgcaa ctgtagaggg cgtcctgctg ttcctgatct tagtggtggt
2041 cgttggaatc ctaatcaaac gaaggagaca gaagatccgg aagtatacga tgcgtaggct
2101 gctgcaggaa actgagttag tggagccgct gacgcccagc ggagcaatgc ccaaccaggc
2161 tcagatgcgg atcctaaaag agacggagct aaggaaggtg aaggtgcttg gatcaggagc
2221 ttttggcact gtctacaagg gcatctggat cccagatggg gagaatgtga aaatccccgt
2281 ggctatcaag gtgttgagag aaaacacatc tcctaaagcc aacaaagaaa ttctagatga
2341 agcgtatgtg atggctggtg tgggttctcc gtatgtgtcc cgcctcctgg gcatctgcct
2401 gacatccaca gtacagctgg tgacacagct tatgccctac ggctgccttc tggaccatgt
2461 ccgagaacac cgaggtcgcc taggctccca ggacctgctc aactggtgtg ttcagattgc
2521 caaggggatg agctacctgg aggacgtgcg gcttgtacac agggacctgg ctgcccggaa
2581 tgtgctagtc aagagtccca accacgtcaa gattacagat ttcgggctgg ctcggctgct
2641 ggacattgat gagacagagt accatgcaga tgggggcaag gtgcccatca aatggatggc
2701 attggaatct attctcagac gccggttcac ccatcagagt gatgtgtgga gctatggagt
2761 gactgtgtgg gagctgatga cttttggggc caaaccttac gatggaatcc cagcccggga
2821 gatccctgat ttgctggaga agggagaacg cctacctcag cctccaatct gcaccattga
2881 tgtctacatg attatggtca aatgttggat gattgactct gaatgtcgcc cgagattccg
2941 ggagttggtg tcagaatttt cacgtatggc gagggacccc cagcgttttg tggtcatcca
3001 gaacgaggac ttgggcccat ccagccccat ggacagtacc ttctaccgtt cactgctgga
3061 agatgatgac atgggtgacc tggtagacgc tgaagagtat ctggtgcccc agcagggatt
3121 cttctccccg gaccctaccc caggcactgg gagcacagcc catagaaggc accgcagctc
3181 gtccaccagg agtggaggtg gtgagctgac actgggcctg gagccctcgg aagaagggcc
3241 ccccagatct ccactggctc cctcggaagg ggctggctcc gatgtgtttg atggtgacct
3301 ggcaatgggg gtaaccaaag ggctgcagag cctctctcca catgacctca gccctctaca
```

FIGURE 16b (SEQ ID NO: 10)

```
3361 gcggtacagc gaggacccca cattacctct gccccccgag actgatggct atgttgctcc
3421 cctggcctgc agcccccagc ccgagtatgt gaaccaatca gaggttcagc ctcagcctcc
3481 tttaacccca gagggtcctc tgcctcctgt ccggcctgct ggtgctactc tagaaagacc
3541 caagactctc tctcctggga agaatggggt tgtcaaagac gtttttgcct tcgggggtgc
3601 tgtggagaac cctgaatact tagtaccgag agaaggcact gcctctccgc cccacccttc
3661 tcctgccttc agcccagcct ttgacaacct ctattactgg gaccagaact catcggagca
3721 ggggcctcca ccaagtaact ttgaagggac ccccactgca gagaaccctg agtacctagg
3781 cctggatgta cctgtatgag acgtgtgcag acgtcctgtg ctttcagagt ggggaaggcc
3841 tgacttgtgg tctccatcgc cacaaagcag ggagagggtc ctctggccac attacatcca
3901 gggcagacgg ctctaccagg aacctgcccc gaggaacctt tccttgctgc ttgaa
```

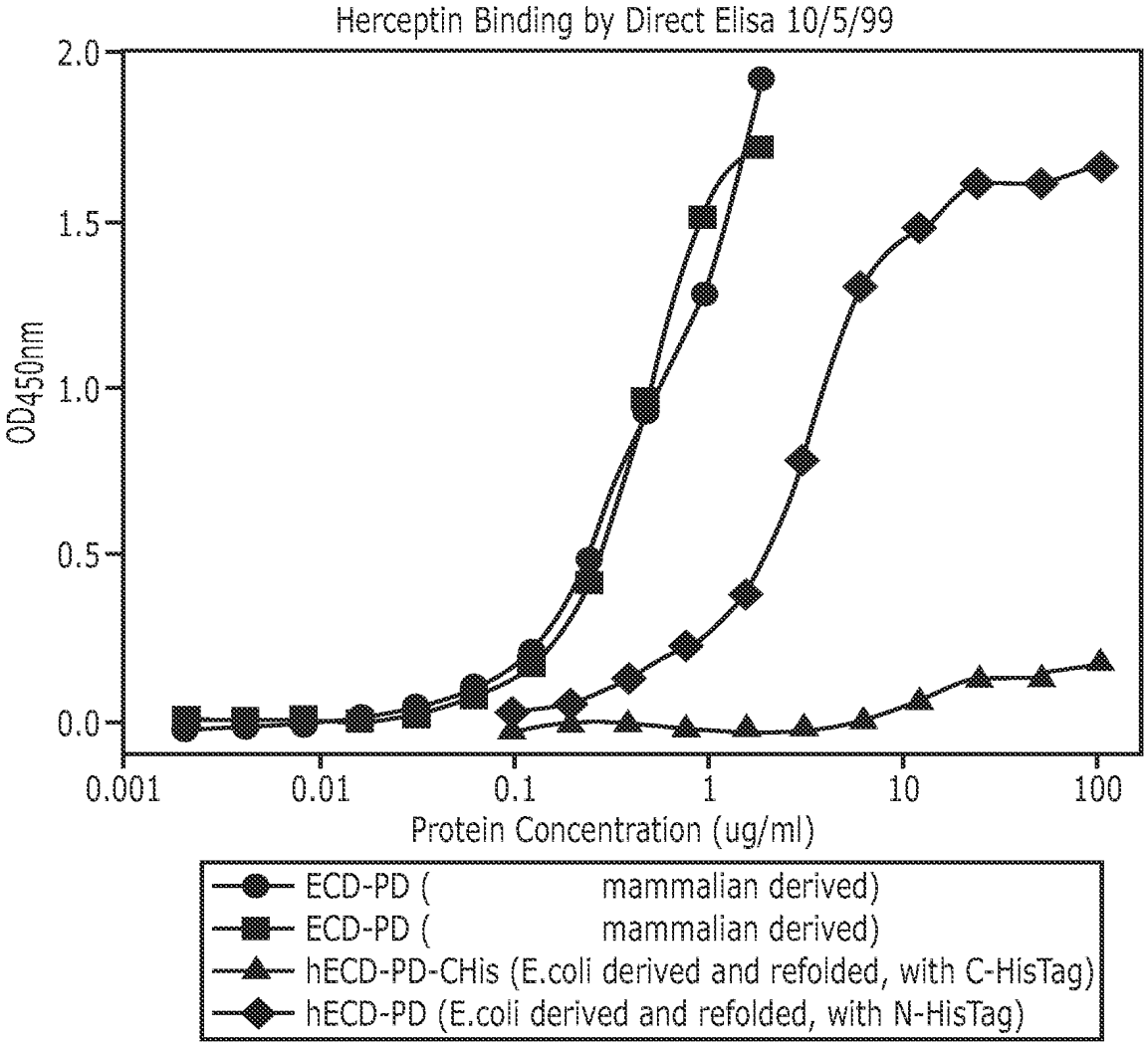
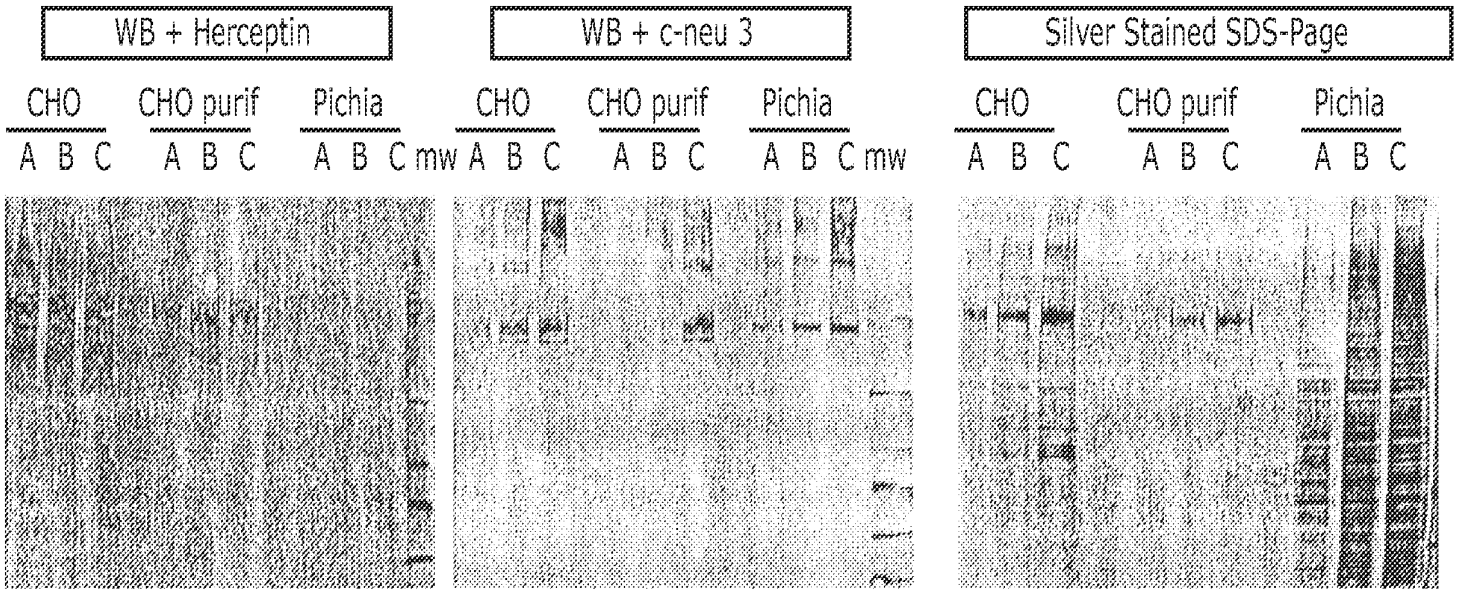

Herceptin Binding by Direct Elisa 10/5/99
2.0
1.5
1.0
0.5
0.0
OD450nm
0.001
0.01
0.1
1
10
100
Protein Concentration (ug/ml)
ECD-PD (mammalian derived)
ECD-PD (mammalian derived)
hECD-PD-CHis (E.coli derived and refolded, with C-HisTag)
hECD-PD (E.coli derived and refolded, with N-HisTag)

FIG. 17

Comparaison of Her2new ECD-PD Expression in CHO-K1 (S/SF) and Pichia (Non reducing conditions)



Legend: CHO; A, B, C = 2,5µl/ 5µl/ 10µl

CHO purif; A, B, C = 125ng/ 250ng/ 500ng

Pichia; A, B, C = 2,5µl/ 5µl/ 10µl from a 1/30 dilution of OD 120

FIG. 18

FIGURE 19a (SEQ ID NO:11)

```
atggagctgg cggcctggtg ccgttggggg ttcctcctcg ccctcctgtc ccccggagcc    60
gcgggtaccc aagtgtgtac cggtaccgac atgaagttgc gactccctgc cagtcctgag   120
acccacctgg acatgcttcg ccacctctac cagggctgtc aggtggtgca gggcaatttg   180
gagcttacct acctgcccgc caatgccagc ctctcattcc tgcaggacat ccaggaagtc   240
cagggataca tgctcatcgc tcacaaccga gtgaaacacg tcccactgca gaggttgcgc   300
atcgtgagag ggactcagct ctttgaggac aagtatgccc tggctgtgct agacaaccga   360
gacccttttgg acaacgtcac caccgccgcc ccaggcagaa ccccagaagg gctgcgggag   420
ctgcagcttc gaagtctcac agagatcttg aagggaggag ttttgatccg tgggaaccct   480
cagctctgct accaggacat ggttttgtgg aaggatgtcc tccgtaagaa taaccagctg   540
gctcctgtcg acatggacac caatcgttcc cgggcctgtc caccttgtgc cccaacctgc   600
aaagacaatc actgttgggg tgagagtcct gaagactgtc agatcttgac tggcaccatc   660
tgtactagtg gctgtgcccg gtgcaagggc cggctgccca ctgactgttg ccatgagcag   720
tgtgctgcag gctgcacggg tcccaagcat tctgactgcc tggcctgcct ccacttcaat   780
catagtggta tctgtgagct gcactgcccg gccctcatca cctacaacac agacaccttc   840
gagtccatgc tcaaccctga gggtcgctac acctttggtg ccagctgtgt gaccacctgc   900
ccctacaact acctctccac ggaagtggga tcctgcactc tggtctgtcc cccgaacaac   960
caagaggtca cagctgagga cggaacacag cggtgtgaga aatgcagcaa gccctgtgct  1020
ggagtatgct atggtctggg catggagcac ctccgagggg cgagggccat caccagtgac  1080
aatatccagg agtttgctgg ctgcaagaag atctttggga gcctggcatt tttgccggag  1140
agctttgatg ggaacccctc ctccggcgtt gccccactga agccagagca tctccaagtg  1200
ttcgaaaccc tggaggagat cacaggttac ctatacattt cagcatggcc agagagcttc  1260
caagacctca gtgtcttcca gaaccttcgg gtcattcggg gacggattct ccatgatggt  1320
gcttactcat tgacgttgca aggcctgggg attcactcac tggggctacg ctcactgcgg  1380
gagctgggca gtggattggc tctcattcac cgcaacaccc atctctgctt tgtaaacact  1440
gtaccttggg accagctctt ccggaacccg caccaggccc tactccacag tgggaaccgg  1500
ccagaagagg catgtggtct tgagggcttg gtctgtaact cactgtgtgc ccgtgggcac  1560
tgctgggggc cagggcccac ccagtgtgtc aactgcagtc agttcctccg gggccaggag  1620
tgtgtggagg agtgccgagt atggaagggg ctccccaggg agtatgtgag gggcaagcac  1680
tgtctgccat gccaccccga gtgtcagcct caaaacagct cggagacctg ctatggatcg  1740
gaggctgacc agtgtgaggc ttgtgcccac tacaaggact catcttcctg tgtggctcgc  1800
tgccccagtg gtgtgaagcc agacctctcc tacatgccta tctggaagta cccggatgag  1860
gagggcatat gtcagccatg ccccatcaac tgcacccact catgtgtgga cctggacgaa  1920
cgaggctgcc cagcagagca gagagccagc ccagtgacat tcatcattgc aactgtggtg  1980
ggcgtcctgt tgttcctgat catagtggtg gtcattggaa tcctaatcaa acgaaggcga  2040
cagaagatcc ggaagtatac catgcgtagg ctgctgcagg agaccgagct ggtggagccg  2100
ctgacgccca gtggagctgt gcccaaccag gctcagatgc ggatcctaaa ggagacagag  2160
ctaaggaagc tgaaggtgct tgggtcagga gccttcggca ctgtctacaa gggcatctgg  2220
atcccagatg gggagaacgt gaaaatcccc gtggccatca aggtgttgag ggaaaacaca  2280
tctcctaaag ctaacaaaga aatcctagat gaagcgtacg tcatggctgg tgtgggttct  2340
ccatatgtgt cccgcctcct gggcatctgc ctgacatcca cagtgcagct ggtgacacag  2400
cttatgccct atggctgcct tctggaccat gtccgagaac accgaggtcg cttaggctcc  2460
caggacctgc tcaactggtg tgttcagatt gccaagggga tgagctacct ggaggaagtt  2520
cggcttgttc acagggacct agctgcccga aacgtgctag tcaagagtcc caaccacgtc  2580
aagattaccg acttcgggct ggcacggctg ctggacattg atgagactga ataccatgca  2640
gatgggggca aggtgcccat caagtggatg gcattggaat ctattctcag acgccggttc  2700
actcatcaga gtgatgtgtg gagctatggt gtgactgtgt gggagctgat gacctttggg  2760
gccaaacctt acgatgggat cccagctcgg gagatccctg atttgctgga gaagggagaa  2820
cgcctacctc agcctccaat ctgcaccatc gacgtctaca tgatcatggt caaatgttgg  2880
atgattgact ccgaatgtcg cccgagattc cgggagttgg tatcagaatt ctcccgtatg  2940
gcaagggacc cccagcgctt tgtggtcatc cagaacgagg acttaggccc ctccagcccc  3000
atggacagca ccttctaccg ttcactgctg gaggatgatg acatgggggga gctggtcgat  3060
gctgaagagt acctggtacc ccagcaggga ttcttctccc cagaccctgc cctaggtact  3120
gggagcacag cccaccgcag acaccgcagc tcgtcggcca ggagtggcgg tggtgagctg  3180
acactgggcc tggagccctc ggaagaagag ccccccagat ctccactggc tccctccgaa  3240
ggggctggct ccgatgtgtt tgatggtgac ctggcagtgg gggtaaccaa aggactgcag  3300
agcctctctc cacatgacct cagccctcta cagcggtaca gtgaggatcc cacattacct  3360
```

FIGURE 19b (SEQ ID NO:11)

```
ctgccccccg agactgatgg ctacgttgct cccctggcct gcagccccca gcccgagtat  3420
gtgaaccagc cagaggttcg gcctcagtct cccttgaccc cagagggtcc tccgcctccc  3480
atccgacctg ctggtgctac tctagaaaga cccaagactc tctctcctgg gaaaaatggg  3540
gttgtcaaag acgtttttgc ctttgggggt gctgtggaga accctgaata cctagcaccc  3600
agagcaggca ctgcctctca gccccaccct tctcctgcct tcagcccagc ctttgacaac  3660
ctctattact gggaccagaa ctcatcggag cagggtcctc caccaagtac ctttgaaggg  3720
acccccactg cagagaaccc tgagtaccta ggcctggatg tgccagtatg a           3771
```

Figure 20a (SEQ ID NO:14)

```
Met Glu Leu Ala Ala Trp Cys Arg Trp Gly Phe Leu Leu Ala Leu Leu
  1               5                  10                  15
Ser Pro Gly Ala Ala Gly Thr Gln Val Cys Thr Gly Thr Asp Met Lys
            20                  25                  30
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
        35                  40                  45
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
    50                  55                  60
Leu Pro Ala Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65                  70                  75                  80
Gln Gly Tyr Met Leu Ile Ala His Asn Arg Val Lys His Val Pro Leu
                85                  90                  95
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Lys Tyr
            100                 105                 110
Ala Leu Ala Val Leu Asp Asn Arg Asp Pro Leu Asp Asn Val Thr Thr
        115                 120                 125
Ala Ala Pro Gly Arg Thr Pro Glu Gly Leu Arg Glu Leu Gln Leu Arg
    130                 135                 140
Ser Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Arg Gly Asn Pro
145                 150                 155                 160
Gln Leu Cys Tyr Gln Asp Met Val Leu Trp Lys Asp Val Leu Arg Lys
                165                 170                 175
Asn Asn Gln Leu Ala Pro Val Asp Met Asp Thr Asn Arg Ser Arg Ala
            180                 185                 190
Cys Pro Pro Cys Ala Pro Thr Cys Lys Asp Asn His Cys Trp Gly Glu
        195                 200                 205
Ser Pro Glu Asp Cys Gln Ile Leu Thr Gly Thr Ile Cys Thr Ser Gly
    210                 215                 220
Cys Ala Arg Cys Lys Gly Arg Leu Pro Thr Asp Cys Cys His Glu Gln
225                 230                 235                 240
Cys Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys
                245                 250                 255
Leu His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu
            260                 265                 270
Ile Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Leu Asn Pro Glu Gly
        275                 280                 285
Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Thr Cys Pro Tyr Asn Tyr
    290                 295                 300
Leu Ser Thr Glu Val Gly Ser Cys Thr Leu Val Cys Pro Pro Asn Asn
305                 310                 315                 320
Gln Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser
                325                 330                 335
Lys Pro Cys Ala Gly Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg
            340                 345                 350
Gly Ala Arg Ala Ile Thr Ser Asp Asn Ile Gln Glu Phe Ala Gly Cys
        355                 360                 365
Lys Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly
    370                 375                 380
Asn Pro Ser Ser Gly Val Ala Pro Leu Lys Pro Glu His Leu Gln Val
385                 390                 395                 400
```

Figure 20b (SEQ ID NO:14)

```
Phe Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp
                405                 410                 415
Pro Glu Ser Phe Gln Asp Leu Ser Val Phe Gln Asn Leu Arg Val Ile
            420                 425                 430
Arg Gly Arg Ile Leu His Asp Gly Ala Tyr Ser Leu Thr Leu Gln Gly
        435                 440                 445
Leu Gly Ile His Ser Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser
    450                 455                 460
Gly Leu Ala Leu Ile His Arg Asn Thr His Leu Cys Phe Val Asn Thr
465                 470                 475                 480
Val Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His
                485                 490                 495
Ser Gly Asn Arg Pro Glu Glu Ala Cys Gly Leu Glu Gly Leu Val Cys
            500                 505                 510
Asn Ser Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln
        515                 520                 525
Cys Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu
    530                 535                 540
Cys Arg Val Trp Lys Gly Leu Pro Arg Glu Tyr Val Arg Gly Lys His
545                 550                 555                 560
Cys Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Ser Ser Glu Thr
                565                 570                 575
Cys Tyr Gly Ser Glu Ala Asp Gln Cys Glu Ala Cys Ala His Tyr Lys
            580                 585                 590
Asp Ser Ser Ser Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp
        595                 600                 605
Leu Ser Tyr Met Pro Ile Trp Lys Tyr Pro Asp Glu Glu Gly Ile Cys
    610                 615                 620
Gln Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Glu
625                 630                 635                 640
Arg Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Val Thr Phe Ile Ile
                645                 650                 655
Ala Thr Val Val Gly Val Leu Leu Phe Leu Ile Ile Val Val Val Ile
            660                 665                 670
Gly Ile Leu Ile Lys Arg Arg Arg Gln Lys Ile Arg Lys Tyr Thr Met
        675                 680                 685
Arg Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser
    690                 695                 700
Gly Ala Val Pro Asn Gln Ala Gln Met Arg Ile Leu Lys Glu Thr Glu
705                 710                 715                 720
Leu Arg Lys Leu Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr
                725                 730                 735
Lys Gly Ile Trp Ile Pro Asp Gly Glu Asn Val Lys Ile Pro Val Ala
            740                 745                 750
Ile Lys Val Leu Arg Glu Asn Thr Ser Pro Lys Ala Asn Lys Glu Ile
        755                 760                 765
Leu Asp Glu Ala Tyr Val Met Ala Gly Val Gly Ser Pro Tyr Val Ser
    770                 775                 780
Arg Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Val Thr Gln
785                 790                 795                 800
Leu Met Pro Tyr Gly Cys Leu Leu Asp His Val Arg Glu His Arg Gly
                805                 810                 815
```

Figure 20c (SEQ ID NO:14)

```
Arg Leu Gly Ser Gln Asp Leu Leu Asn Trp Cys Val Gln Ile Ala Lys
            820                 825                 830
Gly Met Ser Tyr Leu Glu Glu Val Arg Leu Val His Arg Asp Leu Ala
        835                 840                 845
Ala Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys Ile Thr Asp
    850                 855                 860
Phe Gly Leu Ala Arg Leu Leu Asp Ile Asp Glu Thr Glu Tyr His Ala
865                 870                 875                 880
Asp Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu
                885                 890                 895
Arg Arg Arg Phe Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr
            900                 905                 910
Val Trp Glu Leu Met Thr Phe Gly Ala Lys Pro Tyr Asp Gly Ile Pro
        915                 920                 925
Ala Arg Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln
    930                 935                 940
Pro Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp
945                 950                 955                 960
Met Ile Asp Ser Glu Cys Arg Pro Arg Phe Arg Glu Leu Val Ser Glu
                965                 970                 975
Phe Ser Arg Met Ala Arg Asp Pro Gln Arg Phe Val Val Ile Gln Asn
            980                 985                 990
Glu Asp Leu Gly Pro Ser Ser Pro Met Asp Ser Thr Phe Tyr Arg Ser
        995                 1000                1005
Leu Leu Glu Asp Asp Asp Met Gly Glu Leu Val Asp Ala Glu Glu Tyr
    1010                1015                1020
Leu Val Pro Gln Gln Gly Phe Phe Ser Pro Asp Pro Ala Leu Gly Thr
1025                1030                1035                1040
Gly Ser Thr Ala His Arg Arg His Arg Ser Ser Ser Ala Arg Ser Gly
                1045                1050                1055
Gly Gly Glu Leu Thr Leu Gly Leu Glu Pro Ser Glu Glu Glu Pro Pro
            1060                1065                1070
Arg Ser Pro Leu Ala Pro Ser Glu Gly Ala Gly Ser Asp Val Phe Asp
        1075                1080                1085
Gly Asp Leu Ala Val Gly Val Thr Lys Gly Leu Gln Ser Leu Ser Pro
    1090                1095                1100
His Asp Leu Ser Pro Leu Gln Arg Tyr Ser Glu Asp Pro Thr Leu Pro
1105                1110                1115                1120
Leu Pro Pro Glu Thr Asp Gly Tyr Val Ala Pro Leu Ala Cys Ser Pro
                1125                1130                1135
Gln Pro Glu Tyr Val Asn Gln Pro Glu Val Arg Pro Gln Ser Pro Leu
            1140                1145                1150
Thr Pro Glu Gly Pro Pro Pro Pro Ile Arg Pro Ala Gly Ala Thr Leu
        1155                1160                1165
Glu Arg Pro Lys Thr Leu Ser Pro Gly Lys Asn Gly Val Val Lys Asp
    1170                1175                1180
Val Phe Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr Leu Ala Pro
1185                1190                1195                1200
Arg Ala Gly Thr Ala Ser Gln Pro His Pro Ser Pro Ala Phe Ser Pro
                1205                1210                1215
Ala Phe Asp Asn Leu Tyr Tyr Trp Asp Gln Asn Ser Ser Glu Gln Gly
            1220                1225                1230
```

Figure 20d (SEQ ID NO:14)

```
Pro Pro Pro Ser Thr Phe Glu Gly Thr Pro Thr Ala Glu Asn Pro Glu
        1235                1240                1245
Tyr Leu Gly Leu Asp Val Pro Val
    1250                1255
```